REMARKS

This Reply is responsive to the Advisory Action dated March 7, 2005, and the Office Action dated October 21, 2004. Entry of the amendment filed February 3, 2005 is requested in view of the RCE filed concurrently herewith. Accordingly, this amendment and the remarks to follow supplement those previously submitted on February 3, 2005, and full consideration of the amendments and remarks submitted in both amendments is respectfully requested. Entry of the amendments and remarks submitted herein and reconsideration of the claimed subject matter is respectfully requested.

I. Status of the Claims

Claims 1-13 were pending in this application at the time of the Advisory Action dated March 7, 2005. Claims 8 and 10-13 were withdrawn from consideration. Accordingly, claims 1-7 and 9 are now under examination.

II. Amendments to the Claims

Claim 1 has been amended above to delete the word "selected." No prohibited new matter has been added by way of this amendments.

III. Rejections under §112, Second Paragraph and §101

Applicants acknowledge with appreciation the indication in the Advisory Action that Applicants' amendment filed February 3, 2005 is sufficient to overcome the rejections under 35 U.S.C. §112, second paragraph and §101.

IV. Alleged New Matter

In the Advisory Action dated March 7, 2005, the Examiner asserts that several terms in the amended claims do not find support in the specification as filed. For the Examiner's convenience, each rejected term will be addressed individually.

"selected" cellular compartment

The Examiner asserts that the phrase "selected" cellular compartment does not appear to find support in the application as filed. Without necessarily agreeing with the rejection and solely in an effort to expedite allowance, Applicants have deleted the word "selected" from claim 1 by way of amendment above.

"wherein antigen binding capacity is located in a single binding domain" in reference to *"an antibody that is a heavy chain immunoglobulin devoid of a variable light chain domain or an active fragment of said immunoglobulin devoid of a variable light chain domain"*

The Examiner asserts that the phrase "wherein antigen binding capacity is located in a single binding domain" does not appear to find support in the application as filed in reference to "an antibody that is a heavy chain immunoglobulin devoid of a variable light chain domain or an active fragment of said immunoglobulin devoid of a variable light chain domain." Applicants respectfully disagree.

The application as filed provides explicit support for the phrase "wherein antigen binding capacity is located in a single binding domain" at page 8, lines 25-26. In the very

next sentence, at page 8, lines 26-29, the specification states that "[i]t should be understood, however, that isolated VH domains of conventional antibodies are not included within the scope of the invention." This disclosure immediately follows the definition of a "heavy chain immunoglobulin" provided at page 8, lines 11-16, which states that "[a] heavy chain immunoglobulin is an immunoglobulin naturally devoid of any variable light chain domains [where] the antigen-binding capacity and specificity is located exclusively in the immunoglobulin heavy chains" (with emphasis). It would be clear given the above passages, which are disclosed in neighboring paragraphs in the specification, that Applicants' invention concerns the production of heavy chain only antibodies "wherein antigen binding capacity is located in a single binding domain."

Furthermore, in the paragraph directly preceding those discussed above, at page 8, lines 6-9, the term "antibody fragment" is defined as "a portion of a complete antibody which retains the ability to exhibit at least part, and preferably all, of the antigen binding activity." Thus, it would be clear given the above passages, which are disclosed in neighboring paragraphs in the specification, that Applicants' invention also concerns the production of heavy chain only antibody fragments "wherein antigen binding capacity is located in a single binding domain."

"wherein antigen binding capacity is located in a single binding domain" in reference to *"an antibody that is a heavy chain immunoglobulin devoid of a variable light chain domain or an active fragment of said immunoglobulin devoid of a variable light chain domain"*

The Examiner asserts that the phrase "wherein antigen binding capacity is located in a single binding domain" does not appear to find support in the application as filed in reference to "a functional heavy chain antibody or an active fragment of a heavy chain antibody showing the antigen binding activity of the antibody." Applicants respectfully disagree.

As noted above, the application as filed provides explicit support for the phrase "wherein antigen binding capacity is located in a single binding domain" at page 8, lines 25-26. In the very same sentence, the specification states that "[b]y 'functionally equivalent' is meant any protein or fragment or derivative thereof which has the same or similar antigen-binding properties." Furthermore, in the very next sentence as noted above, the specification states that "[i]t should be understood, however, that isolated VH domains of conventional antibodies are not included within the scope of the invention." This disclosure immediately follows the definition of a "heavy chain immunoglobulin" provided at page 8, lines 11-16, which states that "[a] heavy chain immunoglobulin is an immunoglobulin naturally devoid of any variable light chain domains [where] the antigen-binding capacity and specificity is located exclusively in the immunoglobulin heavy chains" (with emphasis). It would be clear given the above passages, which are disclosed in neighboring paragraphs in the specification, that Applicants' invention concerns the production of functional heavy chain only antibodies "wherein antigen binding capacity is located in a single binding domain."

Furthermore, in the paragraph directly preceding those discussed above, at page 8, lines 6-9, the term "antibody fragment" is defined as "a portion of a complete antibody which retains the ability to exhibit at least part, and preferably all, of the antigen binding

activity." Thus, it would be clear given the above passages, which are disclosed in neighboring paragraphs in the specification, that Applicants' invention also concerns the production of functional heavy chain only antibody fragments "wherein antigen binding capacity is located in a single binding domain."

V. Prior Art Rejections

Claims 1, 3, 7, 9 and 14 remain rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Magnuson *et al.* According to the Office Action, the rejection remains because the claims recite no method steps that require the growth of a multicellular plant such that the claims can be distinguished from the method taught by Magnuson, which teaches the production of antibodies in cell suspension. Without agreeing with the rejection and solely in an effort to expedite allowance, Applicants note that claim 1 was amended in the previous amendment filed February 3, 2005, and further amended above, to clarify that the antibodies of the present invention are produced in a cellular compartment in a plant. Reconsideration and withdrawal of the rejection under §102(b) based on Magnuson *et al.* are respectfully requested.

Claims 1, 2, 7, 9 and 14 remain rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Casterman *et al.* According to the Office Action, the rejection is maintained because claims 1, 2, 7 and 9 recite no method steps, and because the claims do not require the production of heavy chain only immunoglobulins that are functional in absence of light chain (Office Action, page 6 and paragraph bridging pages 8-9).

Without agreeing with the rejection and solely in an effort to expedite allowance, Applicants note that claim 1 was amended in the previous amendment filed February 3,

2005 to include the positive process steps of introducing and expressing a DNA sequence encoding the heavy chain antibody in addition to a peptide sequence that targets the antibody to a selected cellular compartment.

With regard to the Examiner's assertion that the heavy chain antibodies referred to in the claims need not be functional, Applicants respectfully disagree. Applicants believe that claim 1 has always made it clear that the antibody or active fragment thereof shows antigen binding activity. Nevertheless, solely to expedite allowance of the present invention, claim 1 was amended in the previous amendment above to clarify that the claimed method produces functional heavy chain antibodies.

With regard to the assertion that the claims do not require the production of heavy chain "only" immunoglobulins, Applicants respectfully disagree. Applicants believe that the statement in claim 1 that the heavy chain antibody is devoid of a variable light chain domain makes it clear that the antibodies are heavy chain only antibodies and not merely heavy chain only antibodies at the point of production. Applicants believe that this would be quite clear when the claim is read in the context of the specification, which states on page 8, lines 26-29, that isolated VH domains of conventional antibodies are not included within the scope of the invention. Nevertheless, solely in an effort to expedite allowance of the present invention, claim 1 was amended in the previous amendment to clarify that the antigen binding capacity of the heavy chain antibodies produced by the present invention resides in a single binding domain.

As the above amendments appear to resolve the reasons provided by the Examiner for maintaining the rejection, Applicants respectfully request reconsideration and withdrawal of the rejection under §102(b) based on Casterman *et al.*

Claim 4 remains rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over either Magnuson *et al.* or Casterman *et al.* in view of Owen *et al.* According to the Office Action, the rejection remains because the claims recite no method steps directed to the production of antibodies in compartments of a real plant. Without agreeing with the rejection and solely in an effort to expedite allowance, Applicants note that claim 4 is dependent on claim 1, which has been amended to clarify that the antibodies of the present invention are produced in a cellular compartment in a plant. Reconsideration and withdrawal of the rejection under §103(a) based on Magnuson *et al.* or Casterman *et al.* in view of Owen *et al.* are respectfully requested.

Claim 5 remains rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over either Magnuson *et al.* or Casterman *et al.* in view of Le Gall *et al.* According to the Office Action, the rejection remains because the claims recite no method steps directed to the production of antibodies in compartments of a real plant. Without agreeing with the rejection and solely in an effort to expedite allowance, Applicants note that claim 5 is dependent on claim 1, which has been amended to clarify that the antibodies of the present invention are produced in a selected cellular compartment in a plant. Reconsideration and withdrawal of the rejection under §103(a) based on Magnuson *et al.* or Casterman *et al.* in view of Le Gall *et al.* are respectfully requested.

Claim 6 was rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over either Magnuson *et al.* or Casterman *et al.* in view of Artsaenko *et al.* According to the Office Action, the rejection remains because the claims recite no method steps directed to the production of antibodies in compartments of a real plant. Without agreeing

with the rejection and solely in an effort to expedite allowance, Applicants note that claim 6 is dependent on claim 1, which has been amended to clarify that the antibodies of the present invention are produced in a cellular compartment in a plant. Reconsideration and withdrawal of the rejection under §103(a) based on Magnuson *et al.* or Casterman *et al.* in view of Artsaenko *et al.* are respectfully requested.

This reply is fully responsive to the Office Action dated October 21, 2004, and the Advisory Action dated March 7, 2005. Accordingly, Applicants respectfully urge that indication of allowable subject matter is now appropriate.

Except for issue fees payable under 37 CFR §1.18, the commissioner is hereby authorized by this paper to charge any additional fees during the pendency of this application including fees due under 37 CFR §1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 CFR §1.136(a)(3).

If the Examiner has any further questions relating to this Reply or to the application in general, she is respectfully requested to contact the undersigned by telephone so that allowance of the present application may be expedited.

Respectfully submitted
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